Population-based health-economic evaluation of the secondary prevention of coronary heart disease in Finland

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of various therapies for the secondary prevention of coronary heart disease in patients who had not met their low-density lipoprotein cholesterol goal of 2.5 mmol/L on simvastatin 40mg. The authors concluded that switching from simvastatin to combination therapy with simvastatin plus ezetimibe 10mg was more cost-effective than switching to generic atorvastatin 20mg or rosuvastatin 10mg. The study was satisfactorily conducted and presented, enhancing the validity of the authors' conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of various statin therapies for the secondary prevention of coronary heart disease in patients who had not met their low-density lipoprotein cholesterol (LDL-C) goal of 2.5 mmol/L on simvastatin 40mg.

Interventions
The therapies were generic atorvastatin 20mg, branded rosuvastatin 10mg, generic simvastatin 40mg, or the combination of generic simvastatin 40mg and branded ezetimibe 10mg.

Location/setting
Finland/primary care.

Methods
Analytical approach:
The analysis was based on a probabilistic decision analytic Markov model with a lifetime horizon. Different populations were considered including patients with or without diabetes, with various serum cholesterol profiles, and of either gender. The authors stated that a societal perspective was adopted.

Effectiveness data:
The epidemiological inputs were from a selection of studies, which were mainly Finnish. Validated risk equations were used to project the population risk of events to the long term. The efficacy of treatment, which was the key input, was from randomised controlled trials identified through a systematic review in the MEDLINE database. The data for switching from simvastatin to simvastatin plus ezetimibe were based on head-to-head clinical trials, while those for the other statins were based on indirect comparisons and some assumptions were needed.

Monetary benefit and utility valuations:
The utility values were from large Finnish studies, using the European Quality of life (EQ-5D) questionnaire and controlling for quality of life with multivariate methods.

Measure of benefit:
Life-years (LYs) and quality-adjusted life-years (QALYs) were the summary benefit measures. QALYs were discounted at an annual rate of 3% and LYs were not discounted.
Cost data:
The economic analysis included the costs of drugs, general practitioner visits, laboratory tests, electrocardiography, treatment of morbidities related to blood pressure and diabetes, and management of fatal and non-fatal events (including travel costs). The drug costs were based on the Finnish Medicine Tariff, while the other health care costs were from the Social Insurance Institution reimbursement data. Event costs were based on national studies and included hospitalisations, drugs, and clinician visits. All costs were in Euros (EUR) and a 3% annual discount rate was applied. The price year was 2007.

Analysis of uncertainty:
A comprehensive probabilistic analysis was undertaken by simultaneously assigning predetermined probability distributions to the model inputs. Cost-effectiveness acceptability curves were generated for various willingness-to-pay (WTP) thresholds. A series of one-way sensitivity analyses was also carried out varying the patient's gender, serum cholesterol profile, or diabetes status.

Results
Both the costs and the QALYs increased consistently when switching from simvastatin to atorvastatin, rosuvastatin, or simvastatin plus ezetimibe, in all subgroups (men, women, diabetic, or non-diabetic). For example, for non-diabetic men, the total costs were EUR 13,032 with simvastatin, EUR 17,067 with atorvastatin, EUR 18,035 with rosuvastatin, and EUR 21,410 with simvastatin plus ezetimibe. The QALYs were 10.488 with simvastatin, 10.635 with atorvastatin, 10.635 with rosuvastatin, and 10,855 with simvastatin plus ezetimibe.

For non-diabetic men, the incremental cost-utility ratio (ICUR) compared with simvastatin, was EUR 27,494 with atorvastatin, EUR 34,096 with rosuvastatin, and EUR 22,841 with simvastatin plus ezetimibe. Rosuvastatin was dominated by atorvastatin and the ICUR with simvastatin plus ezetimibe over atorvastatin was EUR 19,738. The ICUR with simvastatin plus ezetimibe over rosuvastatin was 15,335. Less favourable ICURs were achieved in the non-diabetic female population, while more favourable ratios were achieved in the diabetic population. The incremental cost per LY gained was generally lower for all patient populations and all drugs compared with simvastatin.

The probabilistic analysis suggested that atorvastatin and rosuvastatin were not the best treatments at any WTP threshold. In the male population, the best strategy was remaining on simvastatin at a WTP below EUR 22,842 for non-diabetic patients or EUR 24,018 for diabetic patients, and switching to simvastatin plus ezetimibe at higher values. In the female population, this threshold value was EUR 46,687 for non-diabetic patients or EUR 26,596 for diabetic patients. The baseline LDL-C levels and diabetes status affected the study results, but simvastatin plus ezetimibe was generally more cost-effective than atorvastatin or rosuvastatin, compared with simvastatin.

Authors' conclusions
The authors concluded that switching from generic simvastatin to combination therapy of generic simvastatin plus ezetimibe was more cost-effective than switching to generic atorvastatin or rosuvastatin.

CRD commentary
Interventions:
The selection of comparators was appropriate and included the usual treatment in Finland, as highlighted by the authors.

Effectiveness/benefits:
The approaches used to derive the clinical inputs appear to have been appropriate, as studies that were relevant to the epidemiological setting were selected by the authors, and the treatment efficacy was identified by a systematic review of the literature and the methods and conduct of this review were extensively presented. The reasons for excluding studies that were initially retrieved from the database were reported. The efficacy data were mainly from randomised controlled trials, which should ensure high internal validity. It was necessary to base some data on indirect comparisons, but uncertain estimates were extensively investigated in the sensitivity analyses. Both benefit measures were appropriate as they capture the impact of the disease on both quality of life and survival, which are relevant health dimensions for the patient population. LYs and QALYs also allow cross-disease comparisons. The utility weights were from the Finnish population and collected using appropriate instruments.
Costs:
It was unclear whether the cost categories were consistent with the perspective, because the societal perspective should have included indirect costs, such as productivity losses, which were not included. The authors stated that their approach was in accordance with Finnish guidelines. The data sources were reported and the unit costs were presented for some items, but the disease-related costs were reported as totals and not broken down into individual items. Little information on resource quantities was provided. The price year and the use of discounting were explicitly stated. The probability distributions that were assigned to the economic inputs in the sensitivity analyses were not reported.

Analysis and results:
The results were extensively presented and discussed. Various subgroups of patients were appropriately considered to represent the range of individuals eligible for preventive treatment. The issue of uncertainty was satisfactorily investigated using two approaches. The authors stated that most of their assumptions made to populate the model were conservative against the most efficient treatment (simvastatin plus ezetimibe) and their findings should be considered to be robust. They also stated that their results were based on a validated risk equation and a validated model and could be transferable to settings with similar population risks and costs. This was the first cost-effectiveness analysis of simvastatin plus ezetimibe for the secondary prevention of coronary heart disease that was conducted in Finland.

Concluding remarks:
The study was satisfactorily conducted and presented, enhancing the validity of the authors’ conclusions.

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